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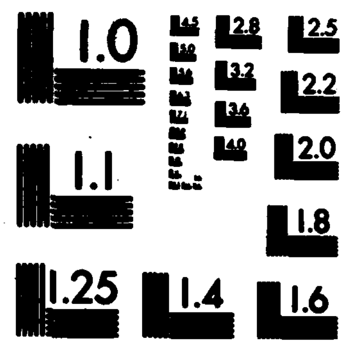

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CELLULAR MECHANISMS OF CENTRAL NERVOUS MODULATION

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AD-A147 878

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Scientific activities

An important aspect of our recent research has been ~~our~~ an attempt to achieve selective disruption of the neuroglia in the central nervous system of our experimental animal, the cockroach (Periplaneta americana). Such selective disruption will be valuable in our research on glial-neurone interactions and also to reveal mechanisms involved in the control of neuroglia during regeneration.

A key technique in our programme is the use of a glial toxin (ethidium bromide), previously used to demyelinate mammalian spinal cords to disrupt selectively the neuroglia of single central nervous connectives, *in vivo*. This has enabled us to distinguish the direct effects on the glia from the associated neuronal damage and changes in the extracellular matrix caused by surgical lesioning.

Such surgical lesioning, which causes extensive axonal changes, results in massive glial proliferation and increased production of extracellular material. Excitability of the giant axons is restored in the proximal stump, but declines within a few days in the distal one where the giant axons are separated from the cell bodies. There is no rapid reformation of normal glial architecture, following transection, and a perineurial blood-brain barrier is not re-established until around 140 days. In contrast, selective disruption with the glial toxin results in rapid restoration of glial structure and function in treated connectives, *in vivo*. This suggests that the presence of undamaged neurones, and/or the framework of the extracellular matrix, are able to direct the reforming cellular elements.

Our preliminary ultrastructure and electrophysiological observations show that the perineurial and underlying glial elements were destroyed by the glial toxin within 24 hours and that axonal excitability was maintained. A consistent feature of the early stages of glial damage was the prominent involvement of granule-containing cells which were never seen in control preparations or in cultured cords treated with glial toxin. In vivo, granule cells appear on the outer surface of the neural lamella and penetrate into the disrupted perineurium. They appear throughout the tissues of ethidium-treated connectives within 24 hours and their numbers increase for up to 4 days. Some of these are clearly phagocytic, but after 48 hours other non-phagocytotic ones form organized layers at the periphery of the connectives. Similar cells were also found deep within the connectives, amongst mesaxonal glia. After 4-6 days, the cells at the surface of the connectives assume a similar morphology to that of the normal perineurium. The non-penetration of extraneous lanthanum, and our electrophysiological observations, show that the peripheral blood-brain barrier is being re-established at this stage. From 6 to 11 days, the cytology of the peripheral cells change progressively. After 28 days they were indistinguishable in ultrastructural and electrophysiological properties from the perineurium of normal, untreated animals.

These preliminary observations suggest that the granule-containing cells, which share a number of cytological features with haemocytes, play an integral part in glial repair. In vertebrates, the blood monocytes have been shown to enter the damaged brain and, it is suggested, are transformed to macrophages. In vertebrates, T-lymphocytes have also been proposed to secrete a glial-growth factor in response to neural damage in addition to any factors released from damaged neurones. Our use of the relatively simple insect central nervous system may, therefore, provide some basic information which will be relevant to the equivalent processes occurring in vertebrate brain.

Publications

Schofield, P.K., Swales, L.S. & Treherne, J.E. (1983) Potentials associated with the blood-brain barrier of an insect: recordings from identified neuroglia. (submitted to J. exp. Biol.).

Schofield, P.K. & Treherne, J.E. (1983). Localization of the blood-brain barrier of an insect: electrical model and analysis. (Submitted to J. exp. Biol.).

Schofield, P.K., Swales, L.S. & Treherne, J.E. (1983). Quantitative analysis of cellular and paracellular effects involved in disruption of the blood-brain barrier of an insect with hypertonic urea. (Submitted to J. exp. Biol.)

Future Research Plans

We propose to use ultrastructural, autoradiographic and electrophysiological methods, together with cell and organ culture techniques, to study the processes of glial regeneration and, in particular, the involvement of haemocytes and the granule containing cells.

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